SUPPORT FOR THE AMENDMENT

Support for the amendment to claims 1, 20, 23 and 34 is found in claim 3 as originally presented. No new matter would be added to this application by entry of this amendment.

Upon entry of this amendment claims 1, 2, 4, 5, 8, 12-14, 20, 23-24, 26-31, 34-35, and 37-42 will now be active in this application with claims 1, 2, 4, 5, 8, 12-14, 23-24, 26-31, 34-35, and 37-42 being under active consideration.

REQUEST FOR RECONSIDERATION

The claimed invention is directed to a method of regulating autonomic nerve activity.

Stimulation of parasympathetic activity over sympathetic activity is believed to reduce stress and calm aggravated mental states, inducing sleep. Oral and percutaneous administration of active ingredients as well as fragrances have been used to improve sleep induction. Some fragrances have been identified as disagreeable or irritating and accordingly new methods for regulating autonomic nerve activity are sought.

The claimed invention addresses this problem by providing a method for regulating autonomic nerve activity such as by increasing an ECG R-R interval, or decreasing systolic and/or diastolic blood pressure, by administering by inhalation, a composition comprising a sesquiterpene alcohol selected from the group consisting of cedrol, cedrenol, globulol and a mixture thereof, wherein the composition has an odor below a detectable threshold. Applicants have discovered that administration by inhalation of such sesquterpene alcohols, in which the composition is such that the odor is below a detectable threshold, is effective for regulating autonomic nerve activity. Such a method is no where disclosed or suggested in the cited prior art of record.

The rejections of claims 1-3, 21-25, 32-36 and 39 under 35 U.S.C. § 103 over Binet et al. in view of Albaugh U.S. 5,095,015, of claims 4, 5, 26, 27, 37 and 38 under 35 U.S.C.

§ 103 in further view of each of Gerard FR 2,697,133, Alburn et al.U.S. 3,632,782 and Nonomura et al. EP 1031348, of claims 13, 14, 30, 31, 41 and 42 in further view of Liu et al. U.S. 5,195,514 are respectfully traversed.

None of the cited references disclose or suggest a method of regulating autonomic nerve activity by administrating by inhalation a composition comprising a sesquiterpene alcohol selected from the group consisting of cedrol, cedrenol, globulol and a mixture thereof, wherein the composition has an odor below a detectable threshold.

Binet describes an investigation into the psychosedative and spasmolytic results by orally or intravenously administering **synthetic farnesol**. Applicants enclose herewith an English language translation of Binet. The reference neither discloses nor suggests a method of administration, a composition comprising a sesquiterpene alcohol selected from the group consisting of cedrol, cedrenol, globulol and a mixture thereof, wherein the composition has an odor below a detectable threshold.

In contrast, the present invention is directed to a method for regulating autonomic nerve activity, by administering by inhalation a composition comprising a sesquiterpene alcohol selected from the group consisting of cedrol, cedrenol, globulol and a mixture thereof, wherein the composition has an odor below a detectable threshold. Applicants note that the claims have been amended to recite using a composition comprising a sesquiterpene alcohol selected from the group consisting of cedrol, cedrenol, globulol and a mixture thereof, wherein the composition has an odor below a detectable threshold.

The examiner cites to Albaugh U.S. 5,095,015 as treating sleep disorders, by administration by inhalation, asserting that it would be obvious to have administered by farnesol of Binet using the administration technique of Albaugh.

Albaugh fails to suggest administration of the farnesol of Binet by inhalation.

Albaugh describes that certain azacycloalkyl imidazopyrimidenes, a new class of GABA brain receptor ligands may be administered by a number of methods, such as orally, topically, parenterally, by inhalation, by spray, or rectally. However, these are enumerated methods for delivery of azocycloalkyl imidazopyrimidene compounds, not terpene compounds. In spite of the common use to treat sleep disorders, the vast differences in chemical structure between the claimed sesquiterpene compounds and the azocycloalkyl imidazopyrimidene compounds of the reference would provide no expectation of success for inhalation by administration of farnesol.

Moreover, Albaugh describes that the azocycloalkyl imidazopyrimidene compounds are specific for the GABA brain receptors and that the disclosed methods of administration are effective for delivery of the specific azocycloalkyl imidazopyrimidenes to the GABA receptors. However, there is no suggestion in Binet as to the action of fanesol and GABA receptors and therefore no motivation to combine the teaching of Albaugh for delivery to GABA receptors with the teaching of Binet for using farnesol to treat sleep disorders.

Moreover, the physiological activity of farnesol is reported to be dependant on the mode of administration and therefore there is no motivation to deviate from the oral and intraperitoneally modes of administration described. Page 903 of the English translation identifies that the acute toxicity of farnesol as being dependant on the manner of administration. Therefore, there would be no motivation to change the identified oral and intraperitoneal modes of administration, to use inhalation as the reference clearly identifies differences in physiological activity based on the mode of administration.

Furthermore, there is no suggestion ot sue a composition having an odor below a detectable threshold. Binet does not describe administration by inhalation and therefore does not suggest using a composition in which the odor is below a detectable threshold. The azocycloalkyl imidazopyrimidene compounds of Albaugh are not describes as having an odor

and therefore do not suggest using a sesquiterpene containing composition which has an odor below a detectable threshold.

For these reasons the claimed invention is not obvious over this combination of references and withdrawal of the rejection under 35 U.S.C. 103(a) is respectfully requested.

The additional teachings of Gerard, Alburn et al. and Nonomura et al do not cure the basic deficiencies of the primary references.

There references have been cited as supportive of the assertion that there is a known physiologic interchangeability of farnesol with other terpene alcohols. However, none of the cited references describe the interchangeability of farnesol with other sesquiterpene alcohols in the area of autonomic nerve regulation and therefore, based on the combined teachings of the cited references there would be no expectation of successfully regulating autonomic nerve activity by administration by inhalation of a terpene alcohol other than farnesol.

Gerard, based on the abstract, appears to describe a composition having bacteriocidal, fungicidal, phytocidal, mollusquicidal and insecticidal activity. Even if the reference were to describe a physiological equivalents for farnesol with other terpenes, such demonstration would not have been in humans and any physiological equivalents would not be expected in humans. None of the organisms for which the physiologic activity of lethal toxicity is demonstrated are even vertebrates or mammals and therefore there would be no expectation of physiological equivalents in humans.

Alburn et al. describes various terpene compounds as useful in treating **influenza viral** infections (column1, lines 30-63). As such, at best the reference describes a similar physiological toxicity in influenza viruses, not in humans or even mammals. There would be no expectation of physiological equivalents in humans.

Nonomura et al. describes certain composition which can inhibit the production of Interleukin-4 (IL-4), which may be useful in treating allergic diseases (pg 2, [0001][0002]).

The composition may contain certain hydroxyl-containing monoterpenes such as l-menthol an citronellole as well as hydroxylated sesquiterpenes such as globuol, epiglobulol, farnesol, guaiol, patchouli alcohol, cedrol, santalol, vetiverol, widrrol, thujopsenol and cedrenol (pg 3 [0015]). However, in spite of the common effect in preventing IL-4 production, there is no suggestion of any equivalence of farnesol with any of cedrol, cedrenol or globulol in an autonomic nerve activity regulation process. There is no disclosed relationship between IL-4 inhibition and regulation of autonomic nerve activity such that there would be no expectation that sesquiterpene alcohols other than farnesol would have the same activity as disclosed by Binet.

While the examiner asserts that it would have been obvious to use a pure form of the farnesol compound in the treatment of sleep disorders, as Binet does not describe administration by inhalation and cedrol typically contains compounds which impart an oder, there would be no motivation to use compounds with an odor below a detectable threshold, in a method in which the composition is administered by inhalation.

As the cited references fail to disclose or suggest a method of administration by inhalation, in which a composition comprising a sesquiterpene alcohol selected from the group consisting of cedrol, cedrenol, globulol and a mixture thereof, wherein the composition an odor below a detectable threshold, the present invention is clearly not obvious from these references and accordingly withdrawal of the rejections under 35 U.S.C. § 103 is respectfully requested.

The rejection of claims 1-5, 8, 12-14 and 21-44 under 35 U.S.C. § 112, first paragraph has been obviated by appropriate amendment.

Applicants respectfully submit that the use of the term "terpene alcohol" is not new matter in view of the specific disclosure of both monoterpene, sesquiterpene and diterpene alcohols. However, the claims have been amended to recite specific alcohol compounds,

identifying the genus as sesquiterpene alcohols, consistent with the original language. Withdrawal of this ground of rejection is respectfully requested.

The rejection of claims 21, 22, 32, 33, 43 and 45 under 35 U.S.C. 112, second paragraph is believed to be moot.

Claims 21, 21, 32, 22, 43 and 44 have been canceled without prejudice.

Applicants submit that this application is now in condition for allowance and early notification of such action is earnestly solicited.

Respectfully submitted,

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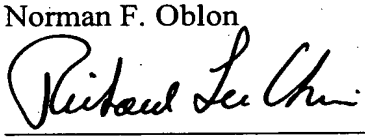

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